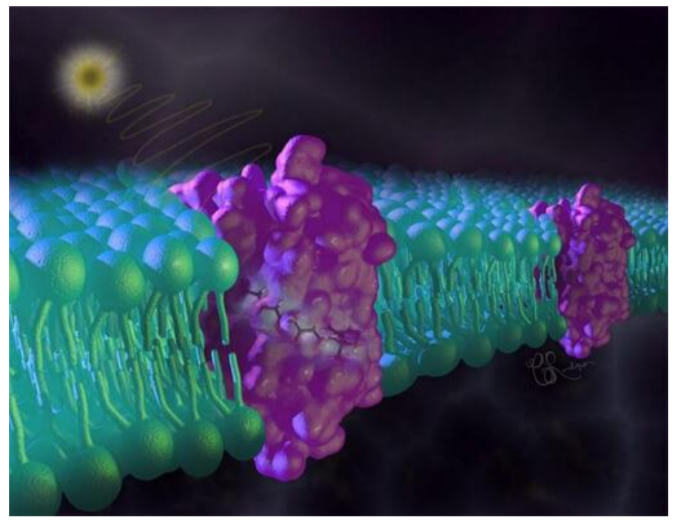


# STRUCTURAL BASIS OF GPCR MODULATION: TOWARDS A NEW CLASS OF MEDICINES?



## WHY

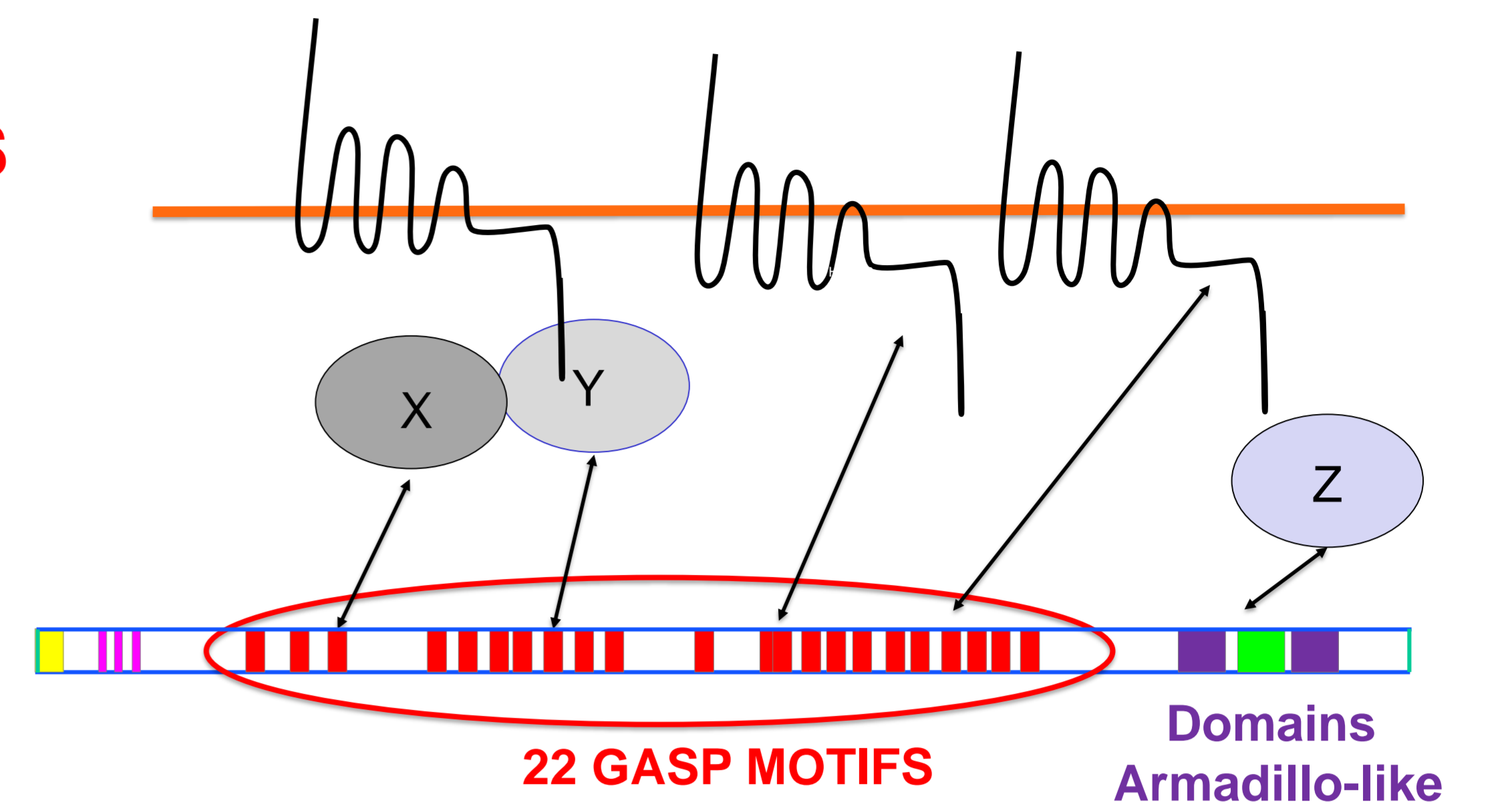


GPCRs (G-protein coupled receptors) are essential players in intercellular communications. GASP (GPCRS-associated sorting proteins) modulate their signalling properties and are implicated in their chronic activation. They serve as scaffolding proteins.



## GOALS

- How do so many different GPCRs recruit GASP proteins and other interactants (X, Y, Z)?
- Can we mimick GASP proteins?



GASP proteins modulate **more than 20 GPCRs** signalling  
But we don't still know how!



**idil**  
INTER-DISCIPLINARY &  
IN-LAB GRADUATE PROGRAM  
UNIVERSITÉ DE MONTPELLIER

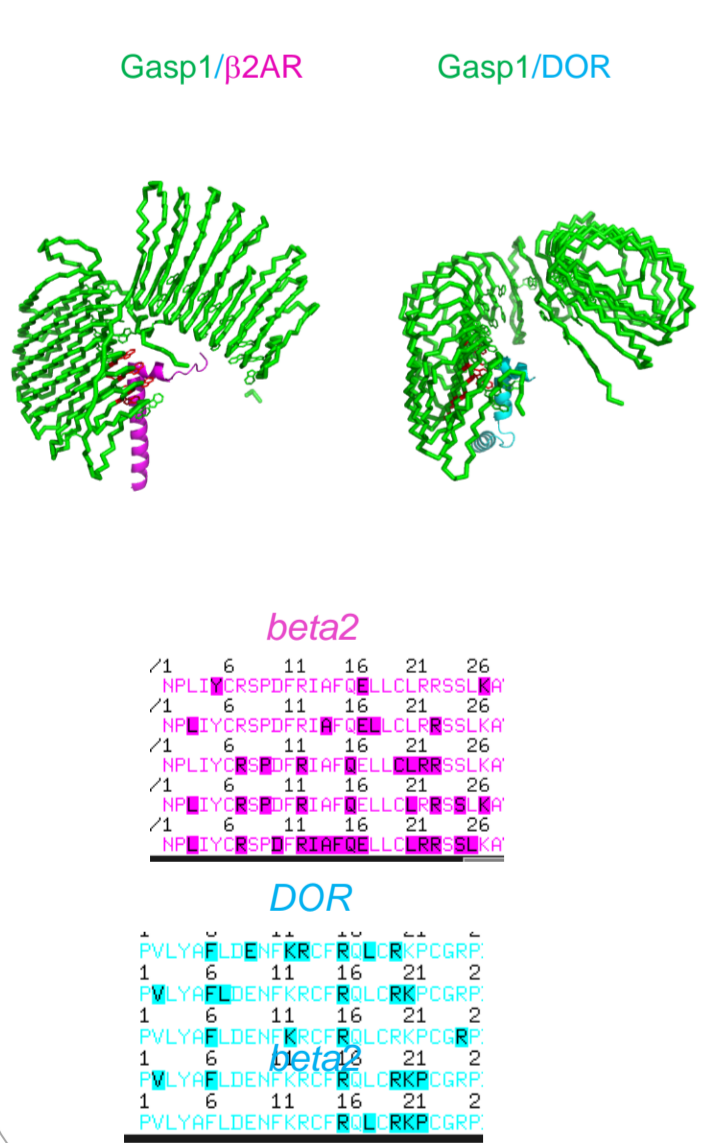


## HOW

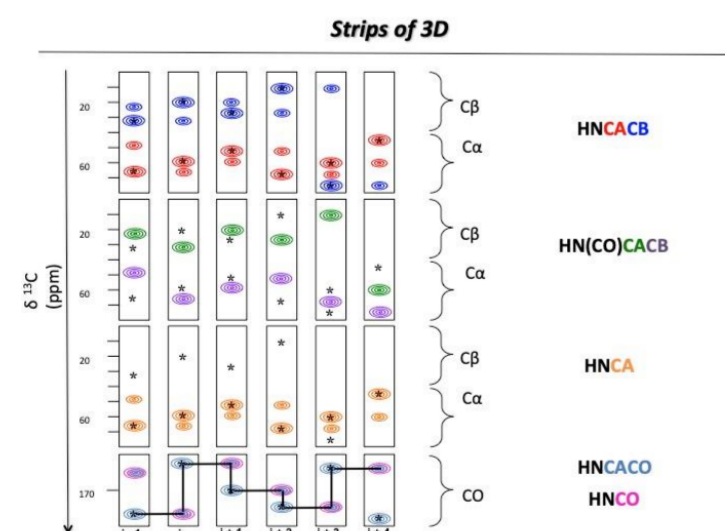
Combining

- extensive AI-based structural prediction
- experimental structural verification (NMR, fluorescence)
- *in vivo* model validation

### In silico prediction



### Production of protein complexes and NMR characterization



## WHO

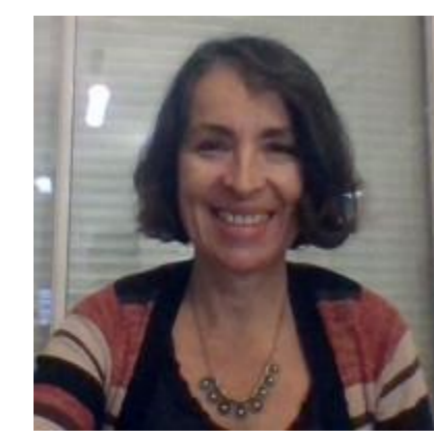
Sandra Lecat  
BSC, Strasbourg



### In vivo assessing

- Construction of biosensors
- Assessing of signalling activity of mutants

Hélène Déméné  
CBS, Montpellier



### Structural studies

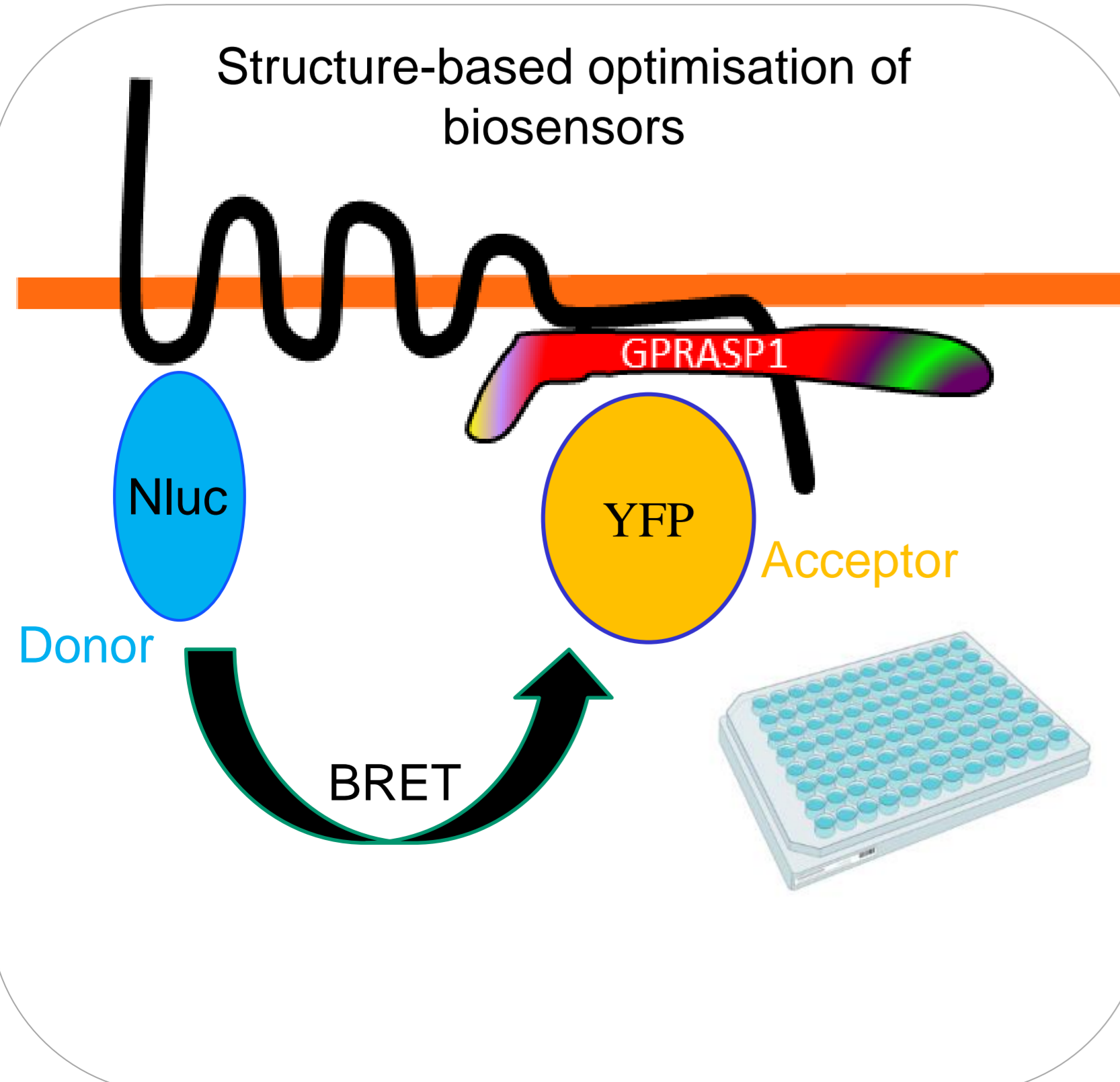
- Extensive Modelling
- NMR

Renaud Wagner  
BSC, Strasbourg



### Production of recombinant proteins

- Subcloning of protein fragments
- Expression in *e-coli* and in yeast



## References

- Abu-Helo et al. *Biomed Pharmacother.* **2025**; 187:118073  
GPRASP1 deletion in mice abrogates adverse side effects associated with chronic stimulation of Beta2-adrenoceptor
- Bornert et al. *PLoS One.* **2013**;8(2):e56336.  
Identification of a novel protein-protein interaction motif mediating interaction of GPCR-associated sorting proteins with G protein-coupled receptors
- Kaeffer et al. *Curr Top Med Chem* **2021**;21(3):227-254.  
GPRASP/ARMCX Protein Family: Potential Involvement in Health and Diseases Revealed by their Novel Interacting Partners
- Simonin et al. *J Neurochem* **2004**; 89(3):766-75  
Identification of a novel family of G protein-coupled receptor associated sorting proteins
- Zeder-Lutz et al. *Anal Biochem.* **2023** 15;665:115062  
Characterization of anti-GASP motif antibodies that inhibit the interaction between GPRASP1 and G protein-coupled receptors